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Supplement to TXR No. 007128-DER for MRID No. 146394. Combined chronic toxicity/carcinogenicity study in rat. This supplement provides a revised and relevant data and Executive Summary to supplement the original DER.

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DATA EVALUATION RECORD

STUDY TYPE: Combined chronic toxicity/carcinogenicity feeding - rat OPPTS 870.4300 [§83-5]; OECD 453.

DP BARCODE: D312641
P.C. CODE: 031401 **TXR NO.:** 0052928

TEST MATERIAL (PURITY): Dichlorprop (95% a.i.)

SYNONYMS: 2,4-Dichlorprop

CITATION: Mitsumori, K. (1984) 2,4-DP Acid (2-(2,4-dichlorophenoxy)propanoic Acid): 24-Month Oral Chronic Dietary Study in Rats: Final Rept. Unpublished study prepared by The Environmental Toxicology Institute. 1069 p. MRID 146394

SPONSOR: Union Carbide Agricultural Products Company

EXECUTIVE SUMMARY:

In a combined chronic toxicity/carcinogenicity study (MRID 146394), dichlorprop (95% a.i., Lot/Batch #: 9/22/80 and 10/31/80) was administered to SPF Fischer 344 rats (80/sex/group) at dietary concentrations of 0, 100, 300, 1000 or 3000 ppm for 104 weeks. The dietary concentrations were equivalent to achieved dosages of 0, 3.6/4.4, 11.0/13.1, 36.5/45.7, and 116147 mg/kg/day in males/females, respectively.

No treatment-related signs of toxicity were observed during daily observations. Survival percentage at the end of 104 weeks was 66, 71, 73, 73, and 70% for males and 66, 75, 66, 73 and 54% for females in the control, 100, 300, 1000, and 3000 ppm groups, respectively. In 3000 ppm groups, both treated males and females showed decreases in body weight (4-11% in males and 10-16% in females), decreases in food efficiency (16% lower than that of the controls) and increased incidences of dark liver and kidneys at necropsy. Evidence of anemia was indicated by

changes in the hematology parameters (decrease in hematocrit, hemoglobin, and erythrocyte counts). The target organs are liver and kidneys. The liver toxicity was based on increased liver weights, changes in clinical chemistry parameters (increases in the levels of alkaline phosphatase, SGPT, and albumin), and histopathological findings (increases in the incidence of diffused hepatocellular swelling in both sexes and increased incidence of lipofuscin deposition in hepatic cells in males). The kidney toxicity was based on increased in the ratios of kidneys to body weights, decreases in specific gravity and protein in urine and increases in lipofuscin deposition in the proximal tubular cells of the kidneys. Slight and non-statistically significant increase in the incidence of liver neoplastic nodules was observed in males (2/80, 2/80, 1/80, 2/80 and 6/80 in the control, 100, 300, 1000, and 3000 ppm groups, respectively); but no treatment-related increase in tumor incidence was found in any organ in either treated males or females.

In 1000 ppm groups, both treated males and females showed decreases in urine specific gravity and protein and increases in lipofuscin deposition in the proximal tubular cells of the kidneys. Increases in the levels of alkaline phosphatase and SGPT were observed in male rats at week 104.

In 300 ppm groups, treated males showed decreases in specific gravity and protein in the urine at weeks 78 and 104. Considering the kidney toxicity seen in the higher dose levels, this effect was considered treatment-related.

The LOAEL is 300 ppm (11/13 mg/kg/day in males/females) based on consistent decreases in specific gravity and protein in the urine. The NOAEL is 100 ppm (3.6/4.4 mg/kg/day in males/females).

No treatment-related increase in tumor incidence was reported. The highest dose tested (3000 ppm) produced liver and kidney toxicity in both males and females and dosing was considered adequate for evaluating the carcinogenic potential for this pesticide.

This chronic toxicity/carcinogenicity study in the rat is **Acceptable/Guideline** and satisfies the guideline requirement for a chronic toxicity/carcinogenicity study in the rat [OPPTS 870.4300); OECD 453].

Survival (%) at terminal sacrifice in rats treated with 2,4-DP in the diet for up to 104 weeks are shown below.

Parameter	Dose (ppm)				
	0	100	300	1000	3000
Males, Terminal Sacrifice	66	71	73	73	70
Females, Terminal Sacrifice	66	75	66	73	54

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